

REMARKS

A. Status of the Claims

Claims 1-18 were examined and remain pending. One paragraph of the specification has been amended to correct an inadvertent typographical error. Claims 1, 7-9 and 16-18 have been amended to address Office concerns raised during a December 18, 2003 telephonic conference with the Examiner and her Primary. No claims have been cancelled. Thus, upon entry of these amendments, claims 1-18 will remain pending.

B. Examiner Interview

Applicants thank Examiner Clow and Primary Examiner Moran for holding a telephone conference with Applicant's representative, Mark Garrett, and Dr. Rama Ranganathan, one of the inventors, on December 18, 2003. The enablement and indefiniteness rejections were discussed.

Examiner Moran explained that the term "statistically significant" in the pending claims was, in the Office's view, sufficiently unclear in scope that the claims were not enabled. Examiner Moran also explained that the Office believed that the metes and bounds of the term "statistically significant" were unclear such that claims 1-9 were indefinite.

Applicant's representative urged that although the term "statistically significant" is broad in that there is more than one way to arrive at a statistically significant conservation energy value as claimed, breadth was not indefiniteness. Applicant's representative also pointed to the text in the specification at lines 14-19 on page 17 as providing support for the meaning of "statistically significant conservation energy values."

Examiner Moran indicated that an issue remained concerning whether the claims complied with section 101 of the patent statute, even though no rejection on that issue was outstanding.

Ultimately, no agreement on the issues discussed was reached. The Office did indicate that it would consider removing the enablement rejection of claims 10-18 in light of Applicants' position that lines 14-19 on page 17 of the specification provided the requisite support for the meaning of "statistically significant conservation energy values."

C. The Claims Are Enabled

The Office maintains its enablement rejection of claims 1-18. Final Office Action at p. 2. The Office made clear during the telephone interview discussed above that it considered the breadth and asserted lack of clarity of the term "statistically significant" within the claim phrase "statistically significant conservation energy values" to be the primary issue underlying the enablement rejection of the claims. It is Applicants' understanding, based on the interview, that if the issues with "statistically significant" are resolved, the enablement rejection will be overcome. Applicants respectfully traverse.

1. Claim 1

Claim 1 has been amended to address the Office's concerns about the term "statistically significant conservation energy values." Claim 1 now requires:

- (b) identifying one or more evolutionarily conserved amino acid positions within the MSA using the following equation:

$$\Delta G_i^{stat} = kT^* \sqrt{\sum_x \left(\ln \frac{P_i^x}{P_{MSA}^x} \right)^2}$$

wherein:

- i is a position in the MSA;
- ΔG_i^{stat} is the conservation energy value for position i;
- P_i^x is the probability of monomer x at position i;
- P_{MSA}^x is the probability of monomer x in the MSA; and
- kT^* is an energy unit, where k is Boltzmann's constant.

In judging enablement, this step must be read in conjunction with the specification, which explains:

“Evolutionarily conserved amino acid positions” refers to particular positions within a multiple sequence alignment which display a non-zero ΔG^{stat} as calculated by Equation 4.

Specification at page 16, lines 6-8. Claims 1-9 are enabled in light of the teachings of the specification generally, and in light of the above-quoted statement in particular, which explains that evolutionarily conserved amino acid positions are positions within an MSA that display a non-zero ΔG^{stat} as calculated by the equation recited in claim 1. The enablement rejection of these claims has been overcome and should be withdrawn.

2. Claim 10

Claim 10 requires:

- (b) calculating a conservation energy value for each position in the MSA using the following equation:

$$\Delta G_i^{stat} = kT^* \sqrt{\sum_x \left(\ln \frac{P_i^x}{P_{MSA}^x} \right)^2}$$

wherein:

i is a position in the MSA;

ΔG_i^{stat} is the conservation energy value for position i ;

P_i^x is the probability of monomer x at position i ;

P_{MSA}^x is the probability of monomer x in the MSA;

kT^* is an energy unit, where k is Boltzmann’s constant; and

- (c) identifying one or more positions within the MSA that have statistically significant conservation energy values.

In judging enablement, these steps must be read in conjunction with the specification, which explains “statistically significant conservation energy values” as follows:

“Statistically significant conservation energy values” may vary with the application. In general, **this refers to values that are greater than the background “noise” value. One manner** of arriving at values that are greater than the background noise is to fit the set of energy values for all positions in an alignment to well-established Gaussian error models. Values greater than two standard deviations from the mean may be classified as “statistically significant.”

Page 17, lines 14-19 (emphasis added).

Thus, the specification explains that the claim phrase “statistically significant conservation energy values,” in general, refers to values that are greater than the background noise value. The specification also explains that when energy values for all positions in a multiple sequence alignment are calculated – as claim 10 requires – **one manner** of arriving at values that are greater than background noise is to fit the set of values to well-established Gaussian error models. Values greater than two standard deviations from the mean are “statistically significant” in such a case.

Applicants submit that claims 10-18 are enabled in light of the teachings of the specification generally, and the above-cited section in particular, and request that the enablement rejection of these claims be withdrawn.

D. Claims 1-9 Are Definite

The Office maintains its indefiniteness rejection of claims 1-9. Final Office Action at p. 6. It is Applicants’ understanding, based on the interview, that the asserted lack of clarity with respect to the “metes and bounds” of the claim term “statistically significant” is the essence of the pending rejection. It also is Applicants’ understanding, based on the interview, that if this issue is adequately addressed, the indefiniteness rejection will be overcome. Applicants respectfully traverse.

Claim 1 has been amended, as set forth above, to remove the phrase “statistically significant conservation energy values.” The scope of the new phrase – “evolutionarily conserved amino acid positions” – is set forth in the specification as:

particular positions within a multiple sequence alignment which display a non-zero ΔG^{stat} as calculated by Equation 4.

Specification at page 16, lines 6-8. Equation 4 is the equation recited in claim 1. Applicants submit that claims 1-9 are definite as amended. *See Miles Lab., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993) (“If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.”). The indefiniteness rejection of these claims should be withdrawn.

E. The Claims Possess Utility

Examiner Moran indicated during the interview that a utility rejection may be forthcoming, although one is not outstanding. She indicated that should such a rejection be issued, it might be based on a notion of the alleged need for one of ordinary skill in the art to be able to “immediately appreciate” why an invention is useful.

There is a statement in the MPEP that “an invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial and credible.” MPEP § 2107 at 2100-29. There is, however, no requirement in the law of such “immediate appreciability” of utility. None appears in *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), or in any case that cites *Brenner*. The Office also should consider that the guidelines that contain the “immediately appreciate” language “do not constitute substantive rulemaking and hence do not have the force and effect of law.” MPEP § 2107 at 2100-29.

In any event, those of ordinary skill in the art will immediately appreciate that both the claimed identification of one or more evolutionarily conserved amino acid positions and the claimed identification of one or more positions having statistically significant conservation energy values are useful.

The threshold for utility is low. The Federal Circuit has explained:

Section 101 of the Patent Act of 1952, 35 U.S.C. § 101, provides that “whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof,” may obtain a patent on the invention or discovery. The threshold of utility is not high: **An invention is “useful” under section 101 if it is capable of providing some identifiable benefit.** See *Brenner v. Manson*, 383 U.S. 519, 534, 16 L. Ed. 2d 69, 86 S. Ct. 1033 (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992) (“To violate § 101 the claimed device must be totally incapable of achieving a useful result”); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention “is incapable of serving any beneficial end”).

Juicy Whip, Inc. v. Orange Bang, Inc., 185 F.3d 1364, 1366 (Fed. Cir. 1999) (emphasis added).

The identification of one or more evolutionarily conserved amino acid positions within an MSA provides an identifiable benefit because conserved positions are well-recognized in the relevant art as valuable information. The following exhibits make this clear:

Tab 1 (Creighton, T.E., *Proteins*, 2nd ed.: 123-125, 1993): The textbook from which this excerpt was taken is intended for undergraduate and graduate students. The excerpt reflects the general acceptance of the principle that conservation indicates functional and structural importance (see highlighted text on page 124);

Tab 2 (Stryer, L., *Biochemistry*, 4th ed.: 433-434, 1997): The biochemistry textbook from which this excerpt was taken is intended for undergraduates. The author makes the point (see highlighted text on page 434) that patterns of conservation are key in predicting important aspects of protein structure and function;

Tab 3 (Shakhnovich, E. *et al.*, *Nature*, 379: 96-98, 1996): The authors of this paper show that identification of conserved residues can help predict the amino acids that are important for protein folding;

Tab 4 (Casari, G., *et al.*, *Structural Biology*, vol. 2, no. 2: 171-178): The authors of this paper conclude that conservation is a good and powerful tool for determining functional residues; and

Tab 5 (Lichtarge, O. *et al.*, *J. Mol. Biol.*, 257: 342-358, 1996): This paper demonstrates the value of calculating conservation in order to identify functional regions of several protein families.

Similarly, the identification of one or more positions within an MSA that have statistically significant conservation energy values provides an identifiable benefit because those one or more positions can be used in the process of identifying, for example, “a) positions in biological sequences that appear to be evolutionarily conserved, and b) positions in biological sequences that appear to interact with one another.” Specification at page 7, lines 7-9. Thus, all of the claims satisfy the utility requirement.

F. Petition for Extension of Time

Pursuant to 37 C.F.R. § 1.136(a), Applicants petition for a three-month extension of time up to and including December 30, 2003 in which to respond to the Office Action dated June 30, 2003. If the check for this extension of time has been omitted, or if any fees are due, the Commissioner is authorized to deduct any fees required for any reason relating to the enclosed materials under 37 C.F.R. §§ 1.16 to 1.21 from Fulbright & Jaworski Deposit Account No.: 50-1212/UTSD:645US/MTG.

G. Conclusion

Applicant respectfully submits that claims 1-18 are in condition for allowance. Should Examiner Clow have any questions, comments, or suggestions relating to this application, she is invited to contact the undersigned attorney at (512) 536-3031.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Mark T. Garrett", written in a cursive style.

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